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10/590,095

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EXAMINER

GOUGH, TIFFANY MAUREEN

ART UNIT

PAPER NUMBER

1657

MAIL DATE

DELIVERY MODE

11/09/2010

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/590,095 | <b>Applicant(s)</b><br>DONATE ET AL. |  |
|                              | <b>Examiner</b><br>TIFFANY M. GOUGH  | <b>Art Unit</b><br>1657              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 26 August 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Applicant's response filed 8/26/2010 has been received and entered into the case.

Claims 1-11 are pending and have been considered on the merits. All arguments and amendments have been considered.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

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not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of each of Baniel (US 3556739) in view of each of Raghavarao et al., (Clean Techn Environ Policy, 2003), Persson et al., (J. Chem Tech Biotechnol, 1999), Ullmann et al. (AIChE Journal vol 41. 1995), Koch (US 4233210) as evidenced by Stephenson (J. Chem. Eng. Data, 1993) and Davison et al., (J. Chem and Eng. Data, 1966).

Applicant claims a method for extracting water from an aqueous solution of a protein comprising the steps of:(a) intermixing the aqueous solution of the protein, an enzyme or a therapeutic protein, with a sufficient quantity of at least one glycol ether at a temperature at least 30 centigrade degrees above the lower critical solution temperature (LCST) to form a suspension comprising a concentrated aqueous protein phase and a liquid organic phase comprising said at least one glycol ether and at least 10 percent water extracted from the aqueous solution of the protein, wherein the glycol ether has an inverse solubility in water, with the proviso that the solubility of the glycol ether in water is significantly less than the solubility of water in the glycol ether, and the glycol ether does not significantly deactivate the protein, and (b) separating the concentrated aqueous protein phase formed in step (a) from at least a portion of the

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liquid organic phase. Applicant claims the intermixing of the glycol ether with the aqueous solution of the protein in step (a) to be conducted at a temperature of from about -5°C to about 70°C. Applicant further claims in step (b), that a portion of the liquid organic phase is allowed to remain with the concentrated aqueous protein phase in an amount from about 1 to about 30 percent by weight or substantially all of the liquid organic phase is separated from the concentrated aqueous protein phase. The method further comprising the steps of: (c) heating the liquid organic phase obtained in step (b) to a temperature which is higher than the temperature in step (a) to form a suspension comprising an aqueous phase and a glycol ether phase, and (d) separating the glycol ether phase formed in step (c) from the aqueous phase., wherein in step (c) the liquid organic phase is heated at a temperature of from about 40°C to about 100°C. Applicant claims the concentrated aqueous protein phase obtained in step (b) is further contacted with a hydrophobic organic solvent and the aqueous phase obtained in step (d) is further contacted with a hydrophobic organic solvent. Applicant claims the glycol ether to be selected from the group consisting of tripropylene glycol ethyl ether, propylene glycol isopropyl ether, dipropylene glycol isopropyl ether, tripropylene glycol isopropyl ether, propylene glycol n-propyl ether, dipropylene glycol n-propyl ether, propylene glycol t-butyl ether, dipropylene glycol t-butyl ether, tripropylene glycol t-butyl ether, propylene glycol n-butyl ether, dipropylene glycol n-butyl ether, tripropylene glycol n-butyl ether, propylene glycol n-pentyl ether, propylene glycol n-hexyl ether, butylene glycol methyl ether, dibutylene glycol methyl ether, butylene glycol ethyl ether and dibutylene glycol ethyl ether, ethylene glycol n-butyl ether, ethylene glycol n-pentyl

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ether, ethylene glycol n-hexyl ether, ethylene glycol n-heptyl ether, ethylene glycol 2-ethylhexyl ether, diethylene glycol n-pentyl ether, diethylene glycol n-hexyl ether, diethylene glycol n-heptyl ether, triethylene glycol n-hexyl ether, ethylene glycol n-butyl ether acetate, propylene glycol isobutyl ether, dipropylene glycol isobutyl ether, tripropylene glycol isobutyl ether, ethylene glycol t-butyl ether, ethylene glycol isobutyl ether, ethylene glycol isobutyl ether acetate, and diethylene glycol n-butyl ether acetate, and blends thereof.

Baniel (US 3556739) teaches an extraction method comprising intermixing an aqueous solution of phosphoric acid with an organic solvent, glycol ether (abstract), at a temperature within the range of -5°C to about 70°C to bring about phase separations, separating the phases, and then heating the liquid organic phase at temperatures higher than the first temperature (col. 2, lines 10-72, col. 3, lines 1-28, 45-col. 4, whole column, col. 5, lines 1-23, example 3, col. 7, lines 1-11). Baniel teaches that the method can be used to extract a product from an aqueous solution with organic solvents like glycol ethers.

Baniel differs from the claimed invention in that they do not teach extracting water from aqueous solutions of proteins.

Raghavarao teach aqueous two phase extraction methods using glycol ethers dependent on cloud point based on temperature (p. 136, introduction). They also teach

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the purification of enzymes and therapeutic proteins (p. 137, second col., p.138, 1<sup>st</sup> col.).

Persson teach the purification of recombinant pharmaceutical proteins using a thermoseparating aqueous two-phase system to recover the target protein from the water phase (abstract). Although Persson teach temperature-phase induced separation using a polymer system, they teach that the two phases are formed by heating an aqueous phase above a critical temperature, i.e. cloud point or LCST, to separate the target protein from the EOPO polymers (p. 239, 1<sup>st</sup> col. , section 2.2, , Fig. 1, p. 240, section 3.1. 3.2). They teach that thermoseparating polymers separate from water solution above a certain temperature, i.e. cloud point or LCST (section 3.1) and that such polymer can be used for bioseparation of proteins (3.2). They teach that such a method is cost-effective and an environmentally favorable downstream process (abstract).

Ullmann teach phase transition extraction methods using solvents with a critical point of miscibility. They teach that with the manipulation of temperature one can create regions where the solvents form two distinct phases. They teach that such method is fast, efficient and improves upon previous extraction methods where the products are often damaged (introduction, p. 4898, whole page).

Koch (US 4233210) teach an protein extraction method comprising precipitating a protein fraction with glycol ether (abstract, col. 2, lines 28-41, col. 3, lines 1-60).

Stephenson and Davison teach the mutual solubilities of water and glycol ethers as well as the lower critical solution temperature.

At the time of the claimed invention, it would have been obvious to one of ordinary skill in the art to use an organic solvent such as glycol ether for aqueous protein extractions because thermoseparating phase separation methods are known in the art to be more cost-effective, fast and preserve the product during the extraction methods as suggested by Raghavarao, Persson, Koch and Ullmann. Further, glycol ethers are known in the art to be used in extraction phase methods as suggested by Baniel and Koch. Given the teachings and inherent properties disclosed by Stephenson and Davison, one of ordinary skill in the art would be capable of determining the temperature to perform such extraction processes as disclosed by Baniel, Raghavarao, Persson and Koch with a reasonable expectation of success in separating a concentrated aqueous protein phase from a liquid organic phase.

### ***Response to Arguments***

Applicant's arguments filed 8/26/2010 have been fully considered but they are not persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was



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within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicant argues that Baniel states that the organic solvents must be extracted from the aqueous phosphoric acid.

Raghavarao et al. teach two phase extraction methods using polyethylene glycols and other water-soluble polymers, not glycol ethers. Glycol ethers are not the same as polyethylene glycols. Glycol ethers are low-molecular weight analogs of polyethylene glycols, but are not the same. Their properties are very different, and because of this they are known as a separate class of compounds. In their abstract, Raghavarao et al. teach that the polymers used in a two aqueous extraction are alternatives to "volatile organic compounds as solvents". Glycol ethers are volatile organic compounds (solvents), not polymers. Accordingly, Ragavarao teaches away from the present invention. Applicants further note that the aqueous two phase extraction as taught by Raghavarao et al. and by Persson et al. is not used to concentrate proteins, but rather to selectively transfer proteins from one aqueous phase (rich in one type of water-soluble polymer or a salt) to another aqueous phase (rich in another type of water-soluble polymer or another salt). Water is present in both phases but water does not transfer between phases. Additionally, Ullmann et al. do not teach concentration of proteins or another organic solute by extraction of water.

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Koch teaches a protein concentration method involving precipitation of the protein fraction by heating followed by treating the precipitated protein solids with glycol ethers and water. Unlike the presently claimed invention, this does not involve extraction of water from an aqueous protein solution to produce a more concentrated aqueous protein solution. Precipitation is a difficult process due to the need to handle a precipitated solid phase.

Davison similarly fails to teach or suggest the present invention ether alone or in combination with any other reference as it combines salt, amines and water. Applicants do not

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

It is the Examiners position that while Baniel teaches phosphoric acid and its transfer into the organic phase, Baniel is relied upon for the teachings of using glycol ethers for temperature phase separations.

Applicants claim 1 is drawn "glycol ether." There is no specific glycol ether claimed and thus glycol ether is given its broadest interpretation. Thus, both Raghavarao and Persson teachings of a glycol ethers meet applicants broad scope of

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glycol ether as defined in claim 1 and Persson even teaches a glycol ether within applicants definition in claim 2.

While Perssons intended use may not be to concentrate proteins, the protein is inherently concentrated as is the extraction of water. Persson teaches purifying proteins using glycol ethers in thermoseparating two-phase systems. Persson teaches that while the protein is in the aqueous water phase, the polymer-rich phase is in equilibrium with the water phase. Thus, water must be extracted from the aqueous protein phase in order to be in equilibrium with the polymer phase, i.e. water transfers along with the polymer into the organic phase. Further, the glycol ether disclosed by Persson falls within the broad scope of claims 1 and 2. The amount of water extraction depends on the specific concentration and type of glycol ether used.

The combination of references is used to show that two phase extractions using glycol ethers in thermoseparating methods to obtain a protein are disclosed in the art. Thus, one of ordinary skill in the art at the time of the claimed invention would have a reasonable expectation of success in separating a concentrated aqueous protein phase from a liquid organic phase using glycol ethers in such methods.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-8, 10-14, 16-20 of copending Application No. 10/590,185. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to methods of extracting proteins from aqueous solution comprising intermixing a solution of protein with glycol ether at temperatures within the same claimed ranges to produce phase separations wherein the protein is recovered. It is noted that the claims of ‘185 require a fermentation broth, however, a fermentation broth is an aqueous solution, therefore anticipated by the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 2, 5, 6, 8, 9, 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1,4,6,7,12 of copending Application No. 10/590,685. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to methods of extracting compounds from aqueous solution comprising intermixing a solution of protein with glycol ether at temperatures within the same claimed ranges to produce phase separations wherein the protein is recovered. It is noted that the claims of '685 are drawn to separating a hydrophilic organic compound; however, proteins are known to be both hydrophilic and hydrophobic compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### ***Response to Arguments***

Applicant wishes to hold the above obviousness-type double patenting rejections in abeyance until allowable subject matter is indicated.

### ***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Shinnar et al. (US 5628906)

Baniel et al. (US 4275234).

Allen et al (Biotechnol. Prog., 2007, vol .23, p. 1163-1170).

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIFFANY M. GOUGH whose telephone number is (571)272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Weber Jon can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Tiffany M Gough/  
Examiner, Art Unit 1657

/Ruth A. Davis/  
Primary Examiner, Art Unit 1651